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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,670	05/07/2002	Audrey Goddard	P3230R1C001-168	7260

30313 7590 05/04/2005

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 05/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,670	EATON ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-13 and 17-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-13 and 17-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/10/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Goddard *et al.*

Date of priority: 10/29/1997

Response to Amendment

The Amendment filed 12-14-2004 in response to the Office Action of 09-10-2004 is acknowledged and has been entered.

Claims 5-13, 17-20 are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Inventorship

In view of the papers filed 12-14-2004, the inventorship in this nonprovisional application has been changed by the deletion of Dan L. Eaton, Ellen Filvaroff, Mary Gerritsen, Christopher J. Grimaldi and Colin Watanabe.

Rejections Maintained:

Claims 5-13, and 17-20 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons of record and for the reasons set forth below:

Applicants respond to the utility rejection by filing an inventor's Declaration (Godowski Declaration) which attests that as of the earliest application to which the present application claims priority, it was known that "enhanced TNF-α levels are beneficial in treating certain conditions, such as cancer and viral infection, and in reducing the deleterious effects of ionizing radiation". Specifically, applicants argue that the Declaration supports the use of the claimed polypeptides "to treat conditions known to be ameliorated by increasing TNF-α levels".

For example, applicant's point to Hallahan *et al.* (Exhibit C) which teaches that an adenoviral vector comprising the TNFα gene was successful in treating tumors in animals. Applicants also note (Goeddel, Exhibit D) that TNFα has been shown to induce necrosis of transplanted tumors, to have cytotoxic properties, and to have anti-viral properties. Additionally, applicants argue that the prior art teaches that TNFα and other cytokines were known to protect against ionizing radiation in the context of radiotherapy (Neta *et al.*, Exhibit E).

In addition to the forgoing scientific literature, the Declaration notes that numerous patents (Exhibits F-J) which relate to the use of TNFα as a therapeutic agent alone or in conjunction with other therapeutically active agents had issued prior to October 29, 1997.

Thus, the Declaration asserts that since the claimed polypeptides can be used to "stimulate release of TNF-α", they can achieve the *same* therapeutic benefits which result from direct administration of TNFα as described in the forgoing references.

These arguments, the Declaration, and the references have been carefully considered but are not found persuasive. For a utility to be "well-established" it must be specific, substantial and credible, and the particulars of a specific and or substantial therapeutic *benefit* with regards to the claimed nucleic acid are inadequately disclosed in the instant specification. In this case,

the specification fails to *correlate* the amount of claimed encoded polypeptide necessary that would predictably provide any sort of therapeutic benefit. For example, the specification designates (page 139-140) some of the PRO polypeptides as "positive" because there was a "higher" amount of TNFα in the PRO polypeptide treated samples compared to the negative control samples. However, it's not clear how this higher amount of TNFα translates into any significant biological value. For example, how does this higher value compare to the normal physiological serum levels of the cytokine? The skilled artisan would only regard a "higher" amount of TNFα as an artifact or an arbitrary value as further experimentation on the claimed material itself would be required in order to determine to what "use" any information regarding this polypeptide could be put.

Furthermore, the forgoing references are not exactly supportive of "general" increases in plasma TNF-α levels. For example, Goeddel *et al.* (Exhibit D) teaches (page 602) that increases in TNF-α can both inhibit the growth of cells and or stimulate the growth of cells. Thus, any proposed therapeutic benefit to increasing serum levels of TNF-α in order to treat tumors is non-specific and speculative at best, because there are many different types of tumor cells and each type may respond in different ways to increased concentrations of TNF-α. This includes stimulating the growth of cancer cells. Further, Goeddel *et al.* also teach (page 600, 1st column) that the expression of TNF-α is "transient" even in the presence of continuous mitogenic simuli. Thus, even though the specification asserts that the claimed polypeptide was "positive" in the assay, the prior art teaches that any corresponding increases in TNF-α are fleeting. Thus, there does not appear to be a substantial utility associated with general increases in TNF-α.

Furthermore, the prior art indicates that TNF-α is highly toxic. Hallahan *et al.* (Exhibit C) teach

(2nd column, page 786) that while TNF-α enhances direct tumor cell killing, it was noted that increased serum concentrations of TNF-α contributed to systemic toxicity and limited the therapeutic efficacy. As set forth previously, the specification only proposes that PRO polypeptides testing positive in this assay are useful for "research purposes" and for therapeutic treatment where enhanced TNF-α release would be beneficial. However, since the assay is essentially flawed as set forth above, and because the art of record does not substantially support general increases in serum levels of TNF-α, it would appear that Applicant's claimed invention is incomplete as further characterization of the polypeptide and the assay would be required in order to determine any therapeutic benefit. Again, the instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. Thus, applicant's arguments have not been found persuasive and the rejection is maintained.

Claims 5-13, and 17-20 remain rejected under 35 U.S.C. 112, first paragraph.

Specifically, since the claimed invention is not supported by either a specific asserted utility or a

well established utility for the reasons set forth above, one skilled in the art clearly would not know how to *use* the claimed invention for the reasons of record.

New Rejections:

Claims 6, and 9-10, are rejected under 35 USC 112, first paragraph, as the specification does not contain a written description of the claimed invention. The limitation of an extracellular domain comprising amino acids 17-234 of SEQ ID NO:6 has no clear support in the specification and the claims as originally filed. Applicant is required to cancel the new matter in the response to this Office Action. Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN

GARY NICKOL
PRIMARY EXAMINER